

# Exhibit A

## **TIMOTHY P. CLACKSON, Ph.D.**

Senior Vice President and Chief Scientific Officer  
ARIAD Pharmaceuticals, Inc.  
26 Landsdowne Street  
Cambridge, MA 02139  
617-494-0400, ext. 258  
clackson@ariad.com

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### **EDUCATION**

1987: B.A. in Biochemistry, First Class Honours. University of Oxford, UK  
1991: Ph.D. in Biology. MRC Laboratory of Molecular Biology, University of Cambridge, UK  
Thesis advisor: Dr Greg Winter  
Thesis title: Antibody engineering using the polymerase chain reaction

### **PROFESSIONAL EXPERIENCE**

1991-1994: Postdoctoral Research, Genentech, Inc., South San Francisco, CA  
Advisor: Dr James A. Wells, Department of Protein Engineering  
1994-present: ARIAD Pharmaceuticals Inc.  
1994: Senior Research Scientist  
1997: Staff Scientist and Project Team Leader  
1999: Principal Scientist and Department Head, Gene Therapy Biology  
1999: Director, Biology Research and Head, Gene Therapy Program  
2000: Vice President, Gene Therapy and Genomics  
2002: Senior Vice President, Science and Technology  
2003: Chief Scientific Officer

### **HONORS AND AWARDS**

1986: Corpus Christi College Scholarship (University of Oxford)  
1987: Oxford University Gibbs Prize for the top degree in Biochemistry  
1987-1990: Emmanuel College External Research Studentship (University of Cambridge)  
1987-1991: UK Medical Research Council (MRC) Research Studentship  
1991-1993: NATO Postdoctoral Research Fellowship

### **PROFESSIONAL ACTIVITIES**

- Editorial Boards/ Advisory Boards: *ACS Chemical Biology*, *Chemical Biology and Drug Design*
- Ad hoc reviewer for *Nature*, *PNAS*, *Nature Biotechnology*, *JACS*, *Chemistry and Biology*, *Biochemistry*, *Angewandte Chemie*, *Journal of Medicinal Chemistry*, *Bio-organic and Medicinal Chemistry*, *Journal of Molecular Biology*, *Protein Engineering*, *BMC Biotechnology*, *Molecular Therapy*, *Journal of Gene Medicine*, *Gene Therapy*, and *Human Gene Therapy*
- Co-Chair, 2004 Gordon Conference on Bioorganic Chemistry
- Member, American Chemical Society; American Association of Cancer Research; American Society of Hematology; American Society of Gene Therapy; UK Biochemical Society
- Member, Board of Tutors in Biochemical Sciences, Harvard University (1995-2000)

## RECENT INVITED LECTURES

- Aug 2007: 13<sup>th</sup> Annual IBC Drug Discovery and Development of Innovative Therapeutics Conference, Boston MA
- Aug 2006: 5th International Congress on Targeted Therapies in Cancer, New York, NY
- Mar 2006: Experimental Biology 2006: Society of Experimental Biology Symposium on Drug Development, San Francisco, CA
- Jan 2006: Seminar Series, Dept. of Chemistry, Tufts University, MA
- Aug 2005: 4th International Congress on Targeted Therapies in Cancer, Washington, DC
- Oct 2004: Keynote Address, Sponsors' Day, Dept. of Chemistry, Penn State University, PA
- Oct 2004: Seminar Series, University of Massachusetts Medical School, Worcester, MA
- Mar 2004: SRI Conference on Protein Interactions, Philadelphia PA
- May 2003: University of Chicago Department of Biochemistry and Molecular Biology, Technology Symposium, Chicago IL
- Apr 2003: American Society of Biochemistry and Molecular Biology (ASBMB), Symposium on Chemical Biology Approaches to Controlling Protein Function; San Diego, CA
- Feb 2003: Mt. Sinai School of Medicine, Carl C. Icahn Center for Gene Therapy and Molecular Medicine seminar series, New York, NY
- Sep 2002: Cardiovascular Research Foundation Transcatheter Cardiovascular Therapeutics (TCT) 2002 Meeting: Drug Eluting Stents Summit, Washington DC
- Aug 2002: American Chemical Society (ACS) Annual Meeting, Eli Lilly Award Symposium on Chemical Biology Approaches to Signaling: Boston, MA
- Jun 2002: Gordon Conference on Bioorganic Chemistry, Proctor Academy, NH
- May 2002: ETH/University of Zurich, Chemical Society Seminar Series, Zurich, Switzerland
- Apr 2002: Pittsburgh Cancer Center, Basic Science Seminar Program; Pittsburgh, PA
- Oct 2001: University of Sussex Department of Biochemistry and Genetics & Development, Seminar series; Brighton, UK
- Oct 2001: Medical College of Wisconsin Dept of Pharmacology and Toxicology, Seminar Series, Milwaukee, WI
- Oct 2001: Yale University Department of Molecular Biophysics and Biochemistry Seminar Program, Yale University, CT
- Sep 2001: European Peptide Society 4<sup>th</sup> Annual Symposium on Peptido- and Proteino-mimetics, Spa, Belgium
- Aug 2001: The Jackson Laboratory, Discovery Strategies 2001 Conference, Novel mechanisms for regulating gene expression in vivo; Portland, ME
- Jun 2001: Gordon Conference on Proteins, Holderness School, NH
- Jan 2001: Rockefeller University Student Sponsored Seminar Series, Rockefeller University, NY
- Aug 2000: 14<sup>th</sup> Annual Meeting of the Protein Society, San Diego, CA
- Jun 2000: International Society of Nephrology, Gene Therapy Symposium, Beaver Creek, CO
- Jun 2000: 3<sup>rd</sup> Annual Meeting of the American Society of Gene Therapy, Denver, CO

## EXTRAMURAL FUNDING

National Institute for Allergy and Infectious Diseases: SBIR Phase I grant 1 R43 AI41317-01: "Design of Rapamycin Analogs with Antifungal Specificity" (1997)

## PUBLICATIONS

### **Original research**

Azam, M., Powers, J.T., Huang, W., Shakespeare, W., Zhu, X., Dalgarno, D., Clackson, T., Sawyer, T.K., & Daley, G.Q. AP24163 inhibits the gatekeeper mutant of BCR/ABL by stabilizing the P-loop dynamics. *Submitted*

Zhou, T., Parillon, L., Huang, W., Wang, Y., Sawyer, T.K., Shakespeare, W.C., Clackson, T., Zhu, X. & Dalgarno, D.C. Structural Analysis of DFG-in and DFG-out Dual Src-Abl Inhibitors Sharing a Common Vinyl Purine Template. *Chem. Biol. Drug Design*, in press

Zheng, C., Voutetakis, A., Metzger, M., Wainer, S., Cotrim, A.P., Eckhaus, M.A., Rivera, V.M., Clackson, T., Chiorini, J.A., Donahue, R.E., Dunbar, C.E. & Baum, B.J. Evaluation of a rapamycin-regulated serotype 2 adeno-associated viral vector in macaque parotid glands. *Oral Diseases*, in press

O'Hare, T., Shakespeare, W.C., Zhu, X., Eide, C.A., Rivera, V.M., Wang, F., Adrian, L.T., Zhou, T., Huang, W., Xu, Q., Metcalf, C.A., Tyner, J.W., Loriaux, M.M., Corbin, A.S., Wardwell, S., Ning, Y., Keats, J.A., Wang, Y., Sundaramoorthi, R., Thomas, M., Zhou, D., Snodgrass, J., Commodore, L., Sawyer, T.K., Dalgarno, D.C., Deininger, M.W.N., Druker, B.J. & Clackson, T. (2009) AP24534, a Pan-BCR-ABL Inhibitor for Chronic Myeloid Leukemia, Potently Inhibits the T315I Mutant and Overcomes Mutation-Based Resistance. *Cancer Cell*, in press

Huang, W., Zhu, X., Wang, Y., Azam, M., Wen, D., Sundaramoorthi, R., Thomas, R.M., Liu, S., Banda, G., Lentini, S.P., Das, S., Xu, Q., Keats, J., Wang, F., Wardwell, S., Ning, Y., Snodgrass, J.T., Broudy, M.I., Russian, K., Daley, G.Q., Iulucci, J., Dalgarno, D.C., Clackson, T., Sawyer, T.K & Shakespeare, W.C. (2009) 9-(Arenethenyl)purines as Dual Src/Abl Inhibitors Targeting the Inactive Conformation: Design, Synthesis and Biological Evaluation. *J. Med. Chem.* 52, 4743-4756.

Wang, Y., Shakespeare, W.C., Huang, W., Sundaramoorthi, R., Lentini, S., Das, S., Liu, S., Banda, G., Wen, D., Zhu, X., Xu, Q., Keats, J., Wang, F., Wardwell, S., Ning, Y., Snodgrass, J.T., Broudy, M.I., Russian, K., Dalgarno, D., Clackson, T. & Sawyer, T.K. (2008). Novel N9-arenethenyl purines as potent dual Src/Abl tyrosine kinase inhibitors. *Bioorg. Med. Chem. Lett.* 18, 4907-4912.

Nguyen, M., Huan-Tu, G., Gonzales-Edick, M., Rivera, V.M., Clackson, T., Jooss, K.U. & Harding, T.C. (2007) Rapamycin-regulated control of anti-angiogenic tumor therapy following rAAV-mediated gene transfer. *Mol. Ther.* 15, 912-920.

Wang, J., Voutetakis, A., Papa, M., Rivera, V.M., Clackson, T., Lodde, B., Mineshiba, F. & Baum, B.J. (2006) Rapamycin control of transgene expression from a single AAV vector in mouse salivary glands. *Gene Ther.* 13, 187-190.

Sanftner, L.M., Rivera, V.M., Suzuki, B.M., Feng, L., Berk, L., Zhou, S., Forsayeth, J.R., Clackson, T. & Cunningham, J. (2006) Dimerizer regulation of AADC expression and behavioral response in AAV-transduced 6-OHDA lesioned rats. *Mol. Ther.* 13, 167-174.

Leberherz, C., Auricchio, A., Maguire, A.M., Rivera, V.M., Tang, W., Grant, R.L., Clackson, T., Bennett, J. & Wilson, J.M. (2005) Long-term inducible gene expression in the eye via adeno-associated virus gene transfer in nonhuman primates. *Human Gene Ther.* 16, 178-86.

Rivera, V.M., Gao, G., Grant, R.L., Schnell, M.A., Zoltick, P.J., Rozamus, L.W., Clackson, T. & Wilson, J.M. (2005) Long-term pharmacologically regulated expression of erythropoietin in primates following

AAV-mediated gene transfer. *Blood* 105, 1424-30.

Kobinger, G.P., Deng, S., Louboutin, J.-P., Vatamaniuk, M., Rivera, V.M., Lian, M.-M., Markmann, J.F., Clackson, T., Raper, S.E., Matschinsky, F. & Wilson, J.M. (2005) Pharmacologically regulated regeneration of functional human pancreatic islets. *Mol. Ther.* 11, 105-11.

O'Hare, T., Pollock, R., Stoffregen, E.P., Keats, J.A., Abdullah, O.M., Moseson, E.M., Rivera, V.M., Tang, H., Metcalf, C.A. III, Bohacek, R.S., Wang, Y., Sundaramoorthi, R., Shakespeare, W.C., Dalgarno, D., Clackson, T., Sawyer, T.K., Deininger, M.W. & Druker, B.J. (2004) Inhibition of wild-type and mutant Bcr-Abl by AP23464, a potent ATP-based oncogenic protein kinase inhibitor: implications for CML. *Blood* 104, 2532-2539.

Richard, R.E., De Claro, R.A., Yan, J., Chien, S., von Recum, H., Morris, J., Kiem, H.-P., Heimfeld, S., Clackson, T., Andrews, R., & Blau, C.A. (2004) Heterogeneity among large animal models of in vivo selection. *Mol. Ther.* 10, 730-740.

Berger, C., Blau, C.A., Huang, M.-L., Iulucci, J.D., Dalgarno, D.C., Gaschet, J., Heimfeld, S., Clackson, T. & Riddell, S.R. (2004) Pharmacologically regulated Fas-mediated death of adoptively transferred T cells in a nonhuman primate model. *Blood* 103, 1261-1269.

Yang, W., Keenan, T.P., Rozamus, L.W., Wang, X., Rivera, V.M., Rollins, C.T., Clackson, T. & Holt, D.A. (2003) Regulation of Gene Expression by Synthetic Dimerizers with Novel Specificity. *Bioorg. Med. Chem. Lett.* 13, 3181-3184.

Crittenden, M., Gough, M., Chester, J., Kottke, T., Thompson, J., Ruchatz, A., Clackson T., Cosset, F.L., Chong, H., Diaz, R.M., Harrington, K., Vallina, L.A. and Vile, R.G. (2003) Pharmacologically regulated production of targeted retrovirus from T cells for systemic anti-tumor gene therapy. *Cancer Res.* 63, 3173-3180.

Johnston, J., Tazelaar, J., Rivera, V.M., Clackson, T., Gao, G.-P. & Wilson, J.M. (2003) Regulated expression of erythropoietin from an AAV vector safely improves the anemia of beta-thalassemia in a mouse model. *Mol. Ther.* 7, 493-497.

Berger, C., Blau, C.A., Clackson, T., Riddell, S.R. & Heimfeld, S. (2003) CD28 costimulation and immunoaffinity-based selection efficiently generate primary gene-modified T cells for adoptive immunotherapy. *Blood* 101, 476-484.

Neff, T., Horn, P.A., Valli, V.E., Gown, A.M., Wardwell, S., Wood, B., von Kalle, C., Peterson, L.J., Morris, J.C., Richard, R.E., Clackson, T., Kiem, H.-P. & Blau, C.A. (2002) Pharmacologically regulated in vivo selection in a large animal. *Blood* 100, 2026-2031.

Auricchio, A., Rivera, V.M., Clackson, T., O'Connor, E.E., Maguire, A.M., Tolentino, M.J., Bennett, J. & Wilson, J.M. (2002) Pharmacological regulation of protein expression from adeno-associated viral vectors in the eye. *Mol. Ther.* 6, 238-242.

Pollock, R., Giel, M., Linher, K. & Clackson, T. Regulation of endogenous gene expression by a small molecule dimerizer. (2002) *Nature Biotech.* 20, 729-733.

Auricchio, A., Gao, G.-P., Yu, Q.C., Raper, S., Rivera, V.M., Clackson, T. & Wilson, J.M. (2002) Constitutive and regulated expression of processed insulin following in vivo hepatic gene transfer. *Gene Ther.* 9, 963-971.

Zhao, S., Zoller, K., Masuko, M., Rojnuckarin, P., Yang, X., Parganas, E., Kaushansky, K., Ihle, J.N., Papayannopoulou, T., Willerford, D.M., Clackson, T. & Blau, C.A. (2002) JAK2, complemented by a

second signal from c-kit or flt-3, triggers extensive self-renewal of primary multipotential hemopoietic cells. *EMBO J.* 21, 2159-2167.

Chong, H., Ruchatz, A., Clackson, T., Rivera, V.M. & Vile, R.G. (2002). A system for small-molecule control of conditionally replication-competent adenoviral vectors. *Mol. Ther.* 5, 195-203.

Iulucci, J.D., Oliver, S.D., Morley, S., Ward, C., Ward, J., Dalgarno, D., Clackson, T. & Berger, H.J. (2001). Intravenous safety and pharmacokinetics of a novel dimerizer drug, AP1903, in healthy volunteers. *J. Clin. Pharmacol.* 41, 870-879.

Thomis, D.C., Marktel, S., Magnani, Z., Traversari, C., Gilman, G., Bordignon, C. & Clackson, T. (2001). A Fas-based suicide switch in human T lymphocytes for treatment of graft-versus-host disease. *Blood* 97, 1249-1257.

Pollock, R., Issner, R., Zoller, K., Natesan, S., Rivera, V.M. & Clackson, T. (2000). Delivery of a stringent rapamycin-regulated gene expression system in a single retroviral vector. *Proc. Natl. Acad. Sci. USA* 97, 13221-13226.

Volchuk, A., Amherdt, M., Ravazzola, M., Brügger, B., Rivera, V.M., Clackson, T., Perrelet, A., Söllner, T.H., Rothman, J.E. & Orci, L. (2000). Mega-vesicles implicated in the rapid transport of intra-cisternal aggregates across the Golgi stack. *Cell* 102, 335-348.

Rollins, C.T., Rivera, V.M., Woolfson, D.N., Keenan, T., Hatada, M., Adams, S.E., Andrade, L.J., Yaeger, D., van Schravendijk, M.R., Holt, D.A., Gilman, M., & Clackson, T. (2000). A ligand-reversible dimerization system for controlling protein-protein interactions. *Proc. Natl. Acad. Sci. USA* 97, 7096-7101.

Yang, W., Rozamus, L.W., Narula, S., Rollins, C.T., Yuan, R., Andrade, L.J., Ram, M.K., Phillips, T.B., van Schravendijk, M.R., Dalgarno, D., Clackson, T. & Holt, D.A. (2000). Investigating protein-ligand interactions with a mutant FKBP possessing a designed specificity pocket. *J. Med. Chem.* 43, 1135-1142.

Rivera, V.M., Wang, X., Wardwell, S., Courage, N., Volchuk, A., Keenan, T., Holt, D.A., Gilman, M., Orci, L., Cerasoli, F., Rothman, J.E. & Clackson, T. (2000). Regulated protein secretion through controlled aggregation in the endoplasmic reticulum. *Science* 287, 826-830.

Keenan, T., Yaeger, D.R., Courage, N.L., Rollins, C.T., Pavone, M.E., Rivera, V.M., Yang, W., Guo, T., Amara, J.F., Clackson, T., Gilman, M. & Holt, D.A. (1998) Synthesis and activity of bivalent FKBP12 ligands for the regulated dimerization of proteins. *Bioorg. Med. Chem.* 6, 1309-35.

Clackson, T., Yang, W., Rozamus, L.W., Hatada, M., Amara, J.F., Rollins, C.T., Stevenson, L.F., Magari, S.R., Wood, S.A., Courage, N.L., Lu, X., Cerasoli, F. Jr., Gilman, M. & Holt, D.A. (1998). Redesigning an FKBP-ligand interface to generate chemical dimerizers with novel specificity. *Proc. Natl. Acad. Sci. USA* 95, 10437-42.

Clackson, T., Ultsch, M.H., Wells, J.A., & de Vos, A.M. (1998). Structural and functional analysis of the 1:1 growth hormone:receptor complex reveals the molecular basis for receptor affinity. *J. Mol. Biol.* 277, 1111-28.

Amara, J.F., Clackson, T., Rivera, V.M., Guo, T., Keenan, T., Natesan, S., Pollock, R., Yang, W., Courage, N.L., Holt, D.A. & Gilman, M. (1997). A versatile synthetic dimerizer for the regulation of protein-protein interactions. *Proc. Natl. Acad. Sci. USA* 94, 10618-23

Rivera, V.M., Clackson, T., Natesan, S., Pollock, R., Amara, J.F., Keenan, T., Magari, S.R., Phillips, T., Courage, N.L., Cerasoli, F., Holt, D.A. & Gilman, M. (1996). A humanized system for the pharmacologic control of gene expression. *Nature Med.* 2, 1028-1032.

Goddard, A.D., Covello, R., Luoh, S.-M., Clackson, T., Attie, K., Gesundheit, N., Rundle, A.C., Wells, J.A. & Carlsson, L.M.S. (1995). Mutations of the growth hormone receptor in children with idiopathic short stature. *New England J. Med.* 333, 1093-1098

Clackson, T. & Wells, J.A. (1995). A hot spot of binding energy in a hormone-receptor interface. *Science* 267, 383-386

Marks, J.D., Griffiths, A.D., Malmquist, M., Clackson, T., Bye, J.M. & Winter, G. (1992). By-passing immunization: building high affinity antibodies by chain shuffling. *Bio/Technology* 10, 779-783

Clackson, T., Hoogenboom, H.R., Griffiths, A.D. & Winter, G. (1991). Making antibody fragments using phage display libraries. *Nature* 352, 624-628

Clackson, T. & Winter, G. (1989). 'Sticky feet' -directed mutagenesis and its application to swapping antibody domains. *Nucleic Acids Res.* 17, 10163-10170

Güssow, D. & Clackson, T. (1989). Direct clone characterization from plaques and colonies by the polymerase chain reaction. *Nucleic Acids Res.* 17, 4000

### ***Review articles, commentaries and book chapters***

Clackson T. (2007) Controlling protein-protein interactions using chemical inducers and disruptors of dimerization. In: *Chemical Biology* (Schreiber, S.L., Kapoor, T. & Wess, G., Eds.) Wiley-VCH, Weinheim, pp.227-249.

Rivera, V.M., Berk, L. & Clackson, T. (2006) Dimerizer-mediated regulation of gene expression. In *Gene Transfer: Delivery and Expression of DNA and RNA* (Friedmann, T. & Rossi, J., eds.), Cold Spring Harbor Press, New York, pp.631-641.

Clackson, T. (2006) Translational research in academia and industry. *Exp. Biol. Med.* 231, 1685-1689.

Clackson, T. (2006) A stability switch for proteins. *Chem. Biol.* 13, 926-928.

Clackson, T. (2006) Dissecting the functions of proteins and pathways using chemically induced dimerization. *Chem. Biol. Drug Des.* 67, 440-442.

Clackson, T. (2006) Breaking and entering. *Nature Chem. Biol.* 2, 14-15.

Russel, M., Lowman, H.B. & Clackson, T. (2004) Introduction to phage biology and phage display. In *Phage Display: A Practical Approach* (Clackson, T. & Lowman, H.B., eds.), Oxford University Press, Oxford, pp. 1-26.

Pollock, R., & Clackson, T. (2002) Dimerizer-regulated gene expression. *Curr. Opin. Biotechnol.* 13, 459-467.

Clackson, T. (2000). Regulated gene expression systems. *Gene Therapy* 7, 120-125.

Clackson, T. (1999). RASSLing with receptors. *Nature Biotechnol.* 17, 131-2.

- Clackson, T. (1998). Redesigning small molecule-protein interfaces. *Curr. Opin. Struct. Biol.* 8, 451-8.
- Clackson, T. (1997). Controlling mammalian gene expression with small molecules. *Curr. Opin. Chem. Biol.* 1, 210-8.
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- Clackson, T. and Wells, J.A. (1994). *In vitro* selection from protein and peptide libraries. *Trends Biotechnol.* 12, 173-184.
- Jackson, R.H., McCafferty, J., Johnson, K.S., Pope, A.R., Roberts, A.J., Chiswell, D.J., Clackson, T., Griffiths, A.D., Hoogenboom, H.R. & Winter, G. (1992). Selection of variants of antibodies and other protein molecules using display on the surface of bacteriophage fd. In *Protein Engineering: A Practical Approach* (Rees, A.R., Sternberg, M.J.E. and Wetzel, R., eds.), IRL Press, Oxford, pp. 277-301
- Clackson, T., Güssow, D. & Jones, P.T. (1991). General applications of PCR to gene cloning and manipulation. In *PCR: A Practical Approach* (McPherson, M.J., Taylor, G.R. and Quirke, P., eds.), IRL Press, Oxford, pp. 187-214

## **Book**

- Clackson, T. & Lowman, H.B., eds. (2004). *Phage Display: A Practical Approach*. Oxford University Press, Oxford.



## PATENTS AND PENDING PATENTS

### ***Issued US patents***

McCafferty, J., Pope, A.R., Johnson, K.S., Hoogenboom, H.R.J., Griffiths, A.D., Jackson, R.H., Holliger, K.P., Marks, J.D., Clackson, T.P., Chiswell, D.J., Winter, G.P. & Bonnert, T. Methods for producing members of specific binding pairs.

US Patent Nos. 5,969,108; 6,172,197; 6,806,079; 6,916,605; 7,063,943

Clackson, T., Gilman, M.Z., Holt, D.A., Keenan, T.P., Rozamus, L & Yang, W. Regulation of biological events using novel compounds.

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Holt, D.A., Keenan, T.P., Clackson, T.P., Rozamus, L., Yang, W. & Gilman, M.Z. Materials and method for treating or preventing pathogenic fungal infection.

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### ***Pending US patent applications***

Clackson, T.P. & Bedrosian, C.L. Therapeutic Materials and Methods. US Pub. App. No. 20060194829

Bedrosian, C.L., Clackson, T.P., & Rivera, V.M. Biomarkers for Evaluating Likelihood of Tumor Sensitivity to an mTOR Inhibitor. US Pub. App. No. 20090215812

Fang, J., Jooss, K., Nguyen, M., Harding, T., Clackson, T.P. & Rivera, V.M.; Regulated expression of recombinant proteins for adeno-associated viral vectors. US Pub. App. No. 20070292922